Remarks

I. Amendments

Claims 1-25 are canceled, and new claims 26-36 are added. The newly added claims do not constitute new matter and are completely supported throughout the specification and originally filed claims.

The specification has been amended at the "Brief Description of the Drawings" to add an inadvertently omitted sequence identifier to the sequence described in Figure 2A. Further, a replacement Figure 2A has been submitted to add this sequence identifier. As the sequence disclosed in Figure 2A is the target putative phosphatase 2C gene represented by SEQ ID NO:1, no new matter has been added. The amendments are supported by the originally filed specification and drawings.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 26-36 are pending in the instant application.

II. Objection to the Specification

The Examiner has objected to the specification because the nucleotide sequence disclosure contained in this application does not comply with the requirements set forth in 37 C.F.R. §§ 1.821-1.825. The Examiner alleges that the sequence in Figure 2A is not identified by a sequence identifier, neither in the figure nor figure legend. Applicant has amended the specification and Figure 2A to add the inadvertently omitted sequence identifier to the putative protein phosphatase 2C gene sequence disclosed as SEQ ID NO:1.

The Applicant contends that Sequence Listing submitted on October 30, 2001, in computer readable format (CRF) and paper, contains all sequences disclosed in the application. Therefore, Applicant believes that a substitute Sequence Listing is not required. Moreover, the content of the paper and computer readable copies of the Sequence Listing submitted on October 30, 2001 are identical. The sequence listing submitted in this application merely presents

nucleotide and/or amino acid sequences that appeared in the application as originally filed in accordance with 37 C.F.R. §1.821-1.825.

II. Rejections

A. *Rejection under 35 U.S.C. § 112, first paragraph*

The Examiner has rejected claims 17-23 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and used the invention commensurate in scope with these claims.

Claims 17-23 are drawn to a transgenic mouse comprising a disruption in a protein phophatase 2C gene which exhibits a phenotype of a stimulus processing disorder or an abnormal startle response, a method of producing the transgenic mouse, a cell derived from the transgenic mouse, and methods of using the transgenic mouse to screen for therapeutic agents.

The Examiner has based his rejection on the alleged "failure of the instant disclosure to provide adequate guidance to make a targeting construct with any other sequence besides the EST set forth in SEQ ID NO:1" and the lack of guidance for generating or using "any knock-out non-human animal or cell in which the endogenouse protein phosphatase 2C (PP2C) gene is simply disrupted without providing a useful phenotype" (see page 5). The Examiner asserts that the claims are broad and encompass any non-human animal, and thus the specific endogenous PP2C sequences of any non-human animal, which the Examiner asserts is not enabled by the instant specification.

Applicant respectfully traverses the rejection. However, Applicant has cancelled claims 17-23, rendering the rejection moot. Therefore, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicant submits that new claims 26-36, which encompass transgenic mice with a particular disruption and phenotype, are fully enabled by the specification and are patentable under 35 U.S.C. § 112, first paragraph.

B. *Rejection under 35 U.S.C. § 112, second paragraph*

Claims 11 and 12 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 11 and 12 are allegedly unclear and confusing in the final step (c). The Examiner asserts that a non-human transgenic animal with a disruption in the protein

phosphatase 2C gene disrupts the expression of the gene and the function of the encoded protein, making it is unclear what expression or function will be determined in the claimed methods.

Applicant respectfully traverses the rejection. However, Applicant has canceled claims 11 and 12. Therefore, the rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant, and Applicant requests its withdrawal. The Applicant submits that new claims 26-36 are definite, and particularly point out and distinctly claim the invention as required by 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 U.S.C. § 103

Claims 1-10 have been rejected by the Examiner as being unpatentable over Capecchi *et al.*, US Patent Serial No. 5,464,764 ("Capecchi") and Hou *et al.*, 1994, *Biochem Mol Biol Int*, 32(4): 773-780 ("Hou").

According to the Examiner, Capecchi teaches positive-negative selection methods and vectors for use in knock-out technology, and allegedly relates to disrupting any gene of interest by generating a targeting construct with two sequences homologous to a gene of interest flanking a positive selection marker. The Examiner acknowledges that Capecchi fails disclose the PP2C gene, and more particularly the gene comprising SEQ ID NO:1 currently recited in the claims, and fails to teach using the disclosed methods to disrupt any PP2C gene, including the putative PP2C gene disclosed in SEQ ID NO:1.

The Examiner alleges that Hou teaches the sequences of two isoforms of PP2C isolated from mouse testis. Hou further relates to various isoforms of PP2C and their expression patterns, which vary among tissues. Hou allegedly proposes that the isoforms may represent different splice variants possibly expressed by different promoters in the various tissues tested. However, Hou clearly fails to teach or suggest the transgenic mice as presently claimed.

The Examiner alleges that it would have been *prima facie* obvious to one having ordinary skill in the art to use the methods described by Capecchi to generate a transgenic mouse comprising a disrupted PP2C gene in the proposed intron sequences to determine whether a single PP2C gene generates the various isoforms as hypothesized by Hou. The Examiner further alleges that one of skill in the art would be motivated to do so in order to determine the physiological effect of altering the expression pattern among the tissues tested to better characterize the function of the various isoforms. Finally, the Examiner asserts that there would have been a reasonable expectation of success to target the PP2C gene disclosed and partially

characterized by Hou using the methods of Capecchi in light of the alleged success with the various genes of interest reduced to practice by Capecchi.

Applicant respectfully traverses the rejection. However, claims 1-10 have been canceled. Therefore, the rejection under 35 U.S.C. § 103 is no longer relevant, and Applicant respectfully requests withdrawal of the rejection.

New claims 26-36 are drawn to a transgenic mouse whose genome comprises a disruption in the putative phoshpatase 2C gene comprising SEQ ID NO:1, methods of making the mouse, cells derived from the mouse, and methods of using the mouse to screen for agents, none of which are obvious in light of the sole or combined teachings of Capecchi and Hou. Moreover, Capecchi and Hou, alone or combined, fail to teach or suggest all of the limitations of these claims, including a specific phenotype resulting from disruption of this particular gene, and especially do not teach or suggest a phenotype of a stimulus processing deficit or an abnormal startle response associated with the disruption. Applicant submits that new claims 26-36 are not obvious in light of the prior art references cited, which is made clear by the Examiner in the Office Action (see pages 15-16).

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-775.

Respectfully submitted,

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